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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/727,855	12/01/2000	Tatsuo Hoshino	20516	4260
7590	04/21/2004		US/(C38435/111694)	
BRYAN CAVE LLP 1290 AVENUE OF THE AMERICAS 33RD FLOOR NEW YORK, NY 10104			EXAMINER NASHED, NASHAAT T	
			ART UNIT 1652	PAPER NUMBER

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/727,855

Applicant(s)

HOSHINO ET AL.

Examiner

Nashaat T. Nashed, Ph. D.

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above claim(s) 8-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 8/6/01, 1/22/02, 3/5/01 & 8/17/01
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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Applicant's election of Group I, claims 1-7, with traverse in the response filed March 24, 2004 is acknowledged. Applicant elected the species of SEQ ID NO: 1. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims 6 and 7 are objected to under 37 CFR § 1.75(d)(1) as being in improper form because the claim states an improper Markush groups. Compounds included within a Markush group must "(1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility." (See MPEP § 803.02.). The mitochondrial superoxide dismutase (MSD), the cytoplasmic superoxide dismutase (CSD), and catalase are independent chemical entity and do not share a common structure feature taught in the specification. Superoxide dismutase and catalase are independent functional activity. Thus, the member of the Markush Group of claim 6 do not share a common structural feature, and function. Similarly, the polynucleotide sequences of SEQ ID NO's: 1-4, 6 and 8 (claim 7) are independent chemical compounds and do not share a common structure feature for the stated utility.

Claims 6 and 7 are objected to because they contain non-elected subject matter.

Claim 2 is objected to because of the word "kingdom" should be replaced with the word "genus". Appropriate correction is required.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,696,293 (293'). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-12 are directed to a method of obtaining a cell with enhanced ability to produce carotenoids by disabling a gene encoding alternative oxidase (AOX), i. e., superoxide dismutase and an oxygen species-quenching factor. The gene encoding the AOX of SEQ ID NO: 2 is isolated from *P. rhodozyma*. It would have been obvious to one of ordinary skill in the art to utilize the claimed cell according to claims 7-12 which is made according to the method of claims 1-6 in a method to make carotenoids (claims 1-6).

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 6, and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to inoperative method. Cultivating a recombinant organism containing disabling mutation to one or more gene encoding "active oxygen species-quenching factor" would not be expected to produce carotenoids, and thus, the claimed method is inoperative. Amending the claim to indicate that the organism is a carotenoids producing would obviate this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 is directed to a method for the production of carotenoids comprising cultivating recombinant organism in which any gene encoding "active oxygen species-quenching factor" is disabled. Claims 2-4 are dependent claims from claim 1 and narrow the scope of the claims to particular organisms. Also, claim 6 is dependent from claim 1 and narrows the claim to specific enzymatic activities, superoxide mutase and catalase. The specification, however, only provides three representative species from *P. rhodozyma*, two superoxide dismutase and catalase. There is no disclosure of any

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particular structure to function/activity relationship among the three disclosed species. The specification also fails to describe additional representative species of these DNAs by any identifying structural characteristics or properties other than the activities recited in claim 6, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to a method for producing carotenoids by culturing *P. rhodozyma* in which the gene(s) encoding mitochondrial and/or cytoplasmic super oxide dismutase and/or catalase has been disabled. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to a method of producing carotenoids using any recombinant organism in which any gene encoding superoxide dismutase activity, catalase, or any other "active oxygen species-quenching factor". Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses a method of producing carotenoids using a recombinant organism in which any gene encoding superoxide dismutase activity, catalase, and/or any other "active oxygen species-quenching factor" has been disabled. Also, the method as claimed is inoperative because the mere cultivating an organism in which a gene(s) has been disabled would not be expected to produce carotenoids. The specification provides guidance and examples in the form of an assay to clone the mitochondrial and cytoplasmic superoxide dismutase as well as partially clone a catalase from *P. rhodozyma*, a carotenoid producing organism, and construct a disabling cosset to produce the recombinant *P. rhodozyma* with disabled gene(s) and the use of the genetically modified *P. rhodozyma* in the production of carotenoids, see examples 1-14. While molecular biological techniques and genetic manipulation to disable specific gene(s) in an organism are known in the prior art and the skill of the artisan are well developed, knowledge regarding the genes is lacking. Thus, searching for any gene encoding "active oxygen species-quenching factor" in any carotenoid producing organism or any host cell comprising a gene cluster required for the biosynthesis of carotenoids is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation required to obtain such a gene is enormous. Since routine experimentation in the art does not include screening number of genomic libraries or

cDNA libraries where the expectation of obtaining the desired gene(s) is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the desired enzymatic activity, the nucleic acid encoding the desired enzymatic activity in any organism, their sequence homologies, and the desired disabling cossets. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

- (a) The phrase "active oxygen species-quenching factor" in claim 1 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. For examination purposes only, it is assumed the phrase referring to any oxidoreductase.
- (b) Claims 1-3, 6, and 7 are incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: recombinant carotenoids producing organism.
- (c) Claims 4 and 5 are included in this rejection because they are dependent on a rejected claim and do not cure its deficiencies.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Nashaat T. Nashed, Ph. D.
Primary Examiner
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